



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : C12N 5/06, 5/08, 5/10, A61K 35/36, A61L 27/00	A3	(11) International Publication Number: WO 99/43787 (43) International Publication Date: 2 September 1999 (02.09.99)
(21) International Application Number: PCT/US99/03859 (22) International Filing Date: 23 February 1999 (23.02.99) (30) Priority Data: 60/075,704 24 February 1998 (24.02.98) US (71) Applicant: ADVANCED TISSUE SCIENCES, INC. [US/US]; 10933 North Torrey Pines Road, La Jolla, CA 92037-1005 (US). (72) Inventors: NAUGHTON, Gail, K.; 10933 North Torrey Pines Road, La Jolla, CA 92037-1005 (US). PINNEY, R., Emmett; 8744 Pagoda Way, San Diego, CA 92126 (US). MANSBRIDGE, Jonathan, N.; 1685 Calle Camille, La Jolla, CA 92037 (US). (74) Agents: CORUZZI, Laura, A. et al.; Pennie & Edmonds LLP, 1155 Avenue of the Americas, New York, NY 10036 (US).		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i> (88) Date of publication of the international search report: 25 November 1999 (25.11.99)
(54) Title: A LIVING CHIMERIC SKIN REPLACEMENT (57) Abstract <p>The invention comprises skin replacements for improved wound healing. In one embodiment, the skin replacement is chimeric and comprises harvesting autologous epithelial cells from a patient and seeding them onto a biocompatible substrate containing allogeneic epithelial cells cultured <i>in vitro</i>. The living chimeric skin replacement may be implanted over a permanent dermal replacement previously implanted at the wound site. In another embodiment the skin replacement is a composite comprising an inner, middle and outer component, comprising (a) an inner component comprising a biocompatible dermal construct having a biodegradable or removable scaffold as a base; (b) a middle component comprising epithelial cells; and (c) an outer component comprising epithelial cells cultured <i>in vitro</i> on a dermal construct comprising a dermal portion having a biodegradable or removable scaffold as a base, said dermal portion being combined with a transitional covering and facing inward toward said middle component of epithelial cells. The invention further comprises methods of making and implanting the various skin replacements of the invention.</p>		

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 99/03859

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12N5/06 C12N5/08 C12N5/10 A61K35/36 A61L27/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C12N A61K A61L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 610 007 A (AUGER F.A. ET AL.) 11 March 1997 (1997-03-11) cited in the application the whole document	1-50
A	ROUABHIA, MAHMOUD: "Skin replacement using chimeric (allogeneic -syngeneic) cultured epidermal sheets." M-S (MEDECINE SCIENCES), (1996) VOL. 12, NO. 12, PP. 1370-1377. , XP002116665 the whole document	1-50
A	WO 97 08295 A (LIFECCELL CORPORATION) 6 March 1997 (1997-03-06) the whole document	1-50
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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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Date of the actual completion of the international search

28 September 1999

Date of mailing of the international search report

12/10/1999

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 99/03859

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 693 332 A (HANSBROUGH J.F.) 2 December 1997 (1997-12-02) cited in the application the whole document ----	1-50
A	US 5 460 939 A (HANSBROUGH J.F. ET AL.) 24 October 1995 (1995-10-24) cited in the application the whole document -----	1-50

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 99/03859

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claims 13-28 and 40-41 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 99/03859

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